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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/049,304	03/27/1998	SAVERIO CARL FALCO	BB-1037-F	5349

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EXAMINER

MCELWAIN, ELIZABETH F

ART UNIT PAPER NUMBER

1638

DATE MAILED: 08/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	09/049,304		FALCO ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Elizabeth McElwain		1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 May 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 8, 10 and 16-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9 and 11-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
     If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \*    c) ☐ None of:  
         1. ☐ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
     \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
     a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>7</u> . | 6) <input type="checkbox"/> Other:  |

Applicant's election without traverse of Group I, claims 1-7, 9 and 11-15 and SEQ ID Nos: 120 and 122, in Paper No. 15 and 20 is acknowledged.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

- 5     The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 3, 6 and 7, and claims 9 and 11-15 dependent thereon, rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is indefinite in the recitation of "or part" with regard to the nucleic acid sequence, since a part can be as little as one nucleotide. Clarification is requested.

Claims 2, 3 and 7 are indefinite in the recitation of "essentially similar" given that it is unclear what the metes and bounds of this term would be regarding the claimed sequences.

- 15     Claim 6 is indefinite in the recitation of "subfragment thereof" with regard to the LKR gene, since a subfragment can be as little as one nucleotide, and the specification fails to define or clarify the use of this term.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

- 20     The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6, 7, 9 and 11-15 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to an isolated nucleic acid fragment comprising a nucleic acid sequence encoding all or part of a lysine ketoglutarate reductase (LKR) and chimeric genes, plant cells and seeds comprising said sequences and methods of using said sequences to reduce LKR in a plant seed. Claims are also drawn to a sequence that is essentially similar to SEQ ID NO: 120 or encoding a protein essentially similar to SEQ ID NO: 122.

However, the specification fails to describe structural features that are essential for LKR activity.

Therefore, it remains unclear what constitutes a nucleic acid sequence encoding an LKR or part of the same. In addition, the specification discusses that LKR sequences have homology to saccharopine dehydrogenases (SDH), and sometimes LKR and SDH are in a single bi-functional protein (pages 31-36). However, no information is provided regarding what structural features would confer either type of enzyme activity.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir.

1997), where it states:

“The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA’s relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA . . . Accordingly, the specification does not provide a written description of the invention . . .”

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, one skilled in the art would not have been in possession of the genus claimed at the time this application was filed.

5           Claims 1-7, 9 and 11-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to an isolated nucleic acid fragment comprising a nucleic acid sequence encoding all or part of a lysine ketoglutarate reductase (LKR) and chimeric genes, plant  
10       cells and seeds comprising said sequences and methods of using said sequences to reduce LKR in a plant seed. Claims are also drawn to a sequence that is essentially similar to SEQ ID NO: 120 or encoding a protein essentially similar to SEQ ID NO: 122. However, the specification does not demonstrate that any of the claimed sequences encode a protein having LKR activity. The specification discusses that LKR sequences have homology to saccharopine dehydrogenases  
15       (SDH), and sometimes LKR and SDH are in a single bi-functional protein (pages 31-36). In addition, the specification discloses that SEQ ID NO:120 and 122 are not full length sequences (page 34). Therefore, it is even more uncertain that the claimed sequences would encode the portions required to confer LKR activity.

20           It is well established that sequence similarity is not sufficient to determine functionality of a DNA coding sequence. See the teachings of Doerks (TIG 14, no. 6: 248-250, June 1998), where it states that computer analysis of genome sequences is flawed, and “overpredictions are

common because the highest scoring database protein does not necessarily share the same or even similar functions” (the last sentence of the first paragraph of page 248). Doerks also teaches homologs that did not have the same catalytic activity because active site residues were not conserved (page 248, the first sentence of the last paragraph). In addition, Smith et al (Nature  
5 Biotechnology 15:1222-1223, November 1997) teach that “there are numerous cases in which proteins of very different functions are homologous” (page 1222, the first sentence of the last paragraph). Also, Brenner (TIG 15, 4:132-133, April 1999) discusses the problem of inferring function from homology, stating that “most homologs must have different molecular and cellular functions” (see the second full paragraph of the second column of page 132, for example).  
10 Furthermore, Borks (TIG 12, 10:425-427, October 1996) teaches numerous problems with the sequence databases that can result in the misinterpretation of sequence data.

Van de Loo et al (AgBiotech News and Information, Vol. 5, No.6: 225N-229N, 1993) teach that sequences encoding fatty acid hydroxylase activity from plants are highly similar to other sequences that do not encode a hydroxylase, but instead encode a fatty acyl desaturase (see  
15 the abstract, at least). In fact, Broun et al teach that as few as four amino acid substitutions can convert an oleate-12 desaturase to a hydroxylase (Science 282: 1315-1317, November 1998). Thus, if sequences are identified only by similarity to DNA encoding a partial sequence of a protein known to encode polyenoic fatty acid isomerase activity, one cannot conclude that these other sequences also encode enzymes having polyenoic fatty acid isomerase activity. In  
20 addition, De Luca teaches that modifying plant biosynthetic pathways by transforming plants with genes encoding enzymes involved in said pathway is highly unpredictable (see the

paragraph bridging the columns on page 225N, for example), and that "on many occasions desired goals have been impossible to achieve" (see the last paragraph on page 228N).

Therefore, both the identification of genes encoding LKR activity, and the modification of LKR activity in a plant seed by transforming a plant with said gene or a portion of said gene are highly unpredictable. Thus, given the uncertainty of a sequence coding for LKR sequences, the lack of working examples, the absence of guidance with regard to identifying a sequence as an LKR, and the breadth of the claims which encompass any sequence encoding an LKR, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.


No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth F. McElwain whose telephone number is (703) 308-1794. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone number for this Group is (703) 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Any inquiry of a general nature or relating to the status of this application should be directed to the legal analyst, Gwendolyn Payne, whose telephone number is (703) 305-2475, or to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth F. McElwain, Ph.D.  
August 2, 2002

  
ELIZABETH F. McELWAIN  
PRIMARY EXAMINER  
GROUP 1600